UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,063	03/09/2006	Stephen Keith Jones	03955.0152USWO	3902

23552 7590 08/28/2009

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,063	JONES ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-22,25,28-31 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-22,25,28-31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/21/2005, 5/6/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-4, 8-22, 25, 28-31 and 33 are pending and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 9, 11-17, 19-22, 25, 28-31 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Handy *et al.* (US 6,997,863).

Handy discloses therapeutic methods for treatment of disease material involving administration of a thermotherapeutic magnetic composition, which contains single domain magnetic particles attached to a target-specific ligand, to a patient and application of an alternating magnetic field to inductively heat the thermotherapeutic magnetic composition (abstract). The term "bioprobe" refers to the composition

comprising a magnetic particle, a biocompatible coating material, and a target-specific ligand (column 6, lines 1-5). Alternating magnetic field frequency is preferably between 100-500 kHz (column 7, line 58 – column 8, line 50). AMF strength is between 20 and 3000 Oe, more preferably 100 and 2000 Oe (column 9, lines 20-25). The size of the magnetic particle such as magnetite (Fe_3O_4) may be from 8 to 20 nm. The size of the bioprobe may be 250 nm (column 12, lines 34+). Suitable materials for coating include synthetic and biological polymers such as acrylates, siloxanes, styrenes, acetates, alkylene glycols, etc. (column 13, lines 5-55). See also Examples 1-22, including FMn2X ferromagnetic particles, poly(methacrylic acid-co-hydroxyethylmethacrylate) coating, dextran shell, etc.

Claims 1-3, 9, 11-22, 25, 28, 29 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Pouliquen ("Magnetite-Dextran Nanocapsules: Preparation and Properties," Microspheres, Microcapsules and Liposomes, 2001, 3, p. 495-523).

Pouliquen discloses magnetic microcapsules composed of iron oxide (magnetite or maghemite) dispersed in polymeric matrix, dextran. The iron oxide can be initially coated with dextran and then dispersed in the matrix (dextran). The size (80-200 nm) of the magnetic microcapsules falls within the claims (see Table 1, page 499). Magnetic polysiloxane microcapsules (0.5-1.0 micron), magnetic polystyrene microcapsules (1.2-3.0 micron) are also disclosed (page 501). Magnetite-starch microcapsules include particles 200 nm, 29.2% iron (page 501). Dextran microcapsules including MDN including 117 nm mean size, iron oxide grains 6 nm are disclosed (page 509). MDNs

may be used for hyperthermia (page 495). Regarding claims 11-13, the recitation "wherein the alternating magnetic field is operated at a frequency in the range of about 100-200 kHz and a field strength of about 60-120 Oe" is not given patentable weight to distinguish over Pouliquen. It is noted that the instant claims art product claims, not method claims.

Claims 1-4, 9, 11-17, 19-22, 25 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Widder *et al.* (US 4,247,406).

Widder discloses intravascularly administratable, magnetically localizable biodegradable carrier comprising microspheres formed from an amino acid polymer matrix with magnetic particles embedded therein (abstract). Microspheres have an average size of less than 1.5 microns and magnetic particles have an average size of not more than 1000 Angstroms. Microspheres may contain from 5-350 parts by weight of magnetic particles per 100 parts of the amino acid polymer (column 2, lines 20-37). For example, microspheres may be 0.5 - 1.5 micron (column 3, line 14). Preferred polymers include albumin, poly-l-glutamic acid, etc. (column 3, lines 60+ - column 7, line 10). Magnetic particles are preferably 50-250 Angstroms, and may include magnetite (column 4, lines 18-38). See also examples. Regarding claims 11-13, the recitation "wherein the alternating magnetic field is operated at a frequency in the range of about 100-200 kHz and a field strength of about 60-120 Oe" is not given patentable weight to distinguish over Pouliquen. It is noted that the instant claims art product claims, not method claims.

Claims 1-4, 9, 11-22, 25 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Chatterjee *et al.* (US 2004/0065969).

Chatterjee discloses microencapsulation methods and products (abstract). A composition is provided which comprises a microencapsulated agent made the methods described herein. For example, in one embodiment, the agent comprises maghemite in the form of nanoparticles having a number average diameter between 5 nm and 50 nm, the matrix material comprises an albumin, and the microparticles have a number average diameter between 300 and 800 nm (paragraph 0012). The agent generally comprises between 5 and 40 wt % of the microparticles. In one embodiment, the agent comprises between 25 and 35 wt % of the microparticles. For example, the amount of magnetic material may depend on how much magnetic strength is desired for the final encapsulated particles (paragraph 0027). Regarding claims 11-13, the recitation "wherein the alternating magnetic field is operated at a frequency in the range of about 100-200 kHz and a field strength of about 60-120 Oe" is not given patentable weight to distinguish over Pouliquen. It is noted that the instant claims art product claims, not method claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 8-22, 25, 28-31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray *et al.* (US 6,167,313) in view of Lesniak *et al.* (US 6,541,039) and Handy *et al.* (US 6,997,863).

Gray discloses a method of site specific treatment of diseased tissue in a patient comprising the steps of i) selecting at least a magnetic material which has a magnetic heating efficiency of at least about $4.5x10^{-8}$ J.m./A.g, when magnetic field conditions are equal to or less than about $7.5x10^{7}$ A/s; (ii) delivering the magnetic material to diseased tissue in a patient; and (iii) exposing the magnetic material in the patient to a linear alternating magnetic field with a frequency of greater than about 10 kHz and a field strength such that the product of field strength, frequency and the radius of the exposed region is less than about $7.5x10^{7}$ A/s to generate hysteresis heat in the diseased tissue (abstract). The magnetic material is preferably gamma-ferric oxide (γFe_2O_3) (column 4, lines 46 - column 5, line 5). The magnetic material is most preferably bound in a matrix material to form a microcapsule. Suitable matrix materials include proteins, polymeric resins such as styrene-divinylbenzene, biopol, albumin, chitosan, etc (column 5, lines

45+). Microcapsules are preferably in the size between 10-100 microns, preferably 30-40 (column 8, lines 20-35), and preferably possess a density in the range of 1 to 5 g/cm3, preferably 1.8-2.2 g/cm^3. In one preferred form, the microcapsules contain cobalt treated gamma Fe_2O_3 particles as the ferromagnetic material, bound together using a **Biopol** matrix. **Using this matrix, magnetic microcapsules in a density range of 1.8-2.2 g/cm^3 and in a size range of 20-50 microns can be obtained** (column 45-51). Albumin may also be used as matrix. Regarding synthetic methods, ferromagnetic particles may be added to a solution containing Biopol in dichloromethane. The mixture is preferably then dropped into a beaker containing poly-vinyl alcohol or the like while being mixed with a homogenising mixer. The mixture should then be left to slowly mix for a suitable period of time to allow the dichloromethane to evaporate. Microcapsules thus formed, may then be washed and size fractionated. Following preparation of the microcapsules, the preparation may be size fractionated to select particles of a preferred size for use in he method of the invention (column 9, lines 1-20).

Gray does not explicitly recite that the magnetic material is in the form of nanoparticles.

Lesniak discloses nanoscale particles suited for use in tumor therapy by hyperthermia. Said particles comprise a preferably superparamagnetic iron oxide containing core and at least two shells surrounding said core (abstract). Iron oxide-containing core includes magnetite, maghemite, etc. and core has an average particle size of 3 to 30 nm (claims 5, 7).

Handy discloses therapeutic methods for treatment of disease material involving administration of a thermotherapeutic magnetic composition, which contains single domain magnetic particles attached to a target-specific ligand, to a patient and application of an alternating magnetic field to inductively heat the thermotherapeutic magnetic composition (abstract). The term "bioprobe" refers to the composition comprising a magnetic particle, a biocompatible coating material, and a target-specific ligand (column 6, lines 1-5). Alternating magnetic field frequency is preferably between 100-500 kHz (column 7, line 58 – column 8, line 50). AMF strength is between 20 and 3000 Oe, more preferably 100 and 2000 Oe (column 9, lines 20-25). The size of the magnetic particle such as magnetite (Fe_3O_4) may be from 8 to 20 nm. The size fo the bioprobe may be 250 nm (column 12, lines 34+). Suitable materials for coating include synthetic and biological polymers such as acrylates, siloxanes, styrenes, acetates, alkylene glycols, etc. (column 13, lines 5-55). See also Examples 1-22, including FMn2X ferromagnetic particles, poly(methacrylic acid-co-hydroxyethylmethacrylate) coating, dextran shell, etc.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ nanoscale maghemite particles, such as particles less than 30 nm in size in the methods of Gray when the teaching of Gray is taken in view of Lesniak and Handy. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because Gray teaches that superparamagnetic single domain particles are used as the magnetic material, including gamma ferric oxide, Fe_2O_3 (column 4, lines 63+), and because Lesniak teaches that

particle size of not more than 30 nm is usually a prerequisite for superparamagnetism (column 3, lines 60+). With regard to claimed frequency and field strength of the alternating magnetic field used in hyperthermia treatment, Handy shows frequency and field strength known in the art to be useful for such methods. Regarding claims 2-4, while Gray does not specifically recite percentage of maghemite in the microcapsules, it is interpreted absent evidence to the contrary that the microcapsules of Gray would inherently be capable of having the claimed volume fraction of magnetic material and would be capable of achieving the claimed value because Gray teaches particles having the same material components and same density (e.g. 1-5 g/cm^3, preferably 1.8-2.2 g/cm^3 (column 8, lines 37-42). Since the density of the particles is directly related to the respective amounts of magnetic particle and matrix polymer present within the microcapsule, a microcapsule comprising the same materials (e.g. maghemite and biopol or PVA) and having the same size and density would thus have the claimed volume fraction of magnetic material. Regarding claim 10, Gray teaches microcapsules having the same size, density, and material components as those claimed and exemplified in Applicant's specification (e.g. maghemite and biopol or PVA), thus absent evidence to the contrary the microcapsules would inherently be capable of achieving the claimed VAR values upon exposure to alternating magnetic field. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d

705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Claims 1-4, 8-22, 25, 28-31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jones *et al.* (*Phys. Med. Biol.*, 2001, 46, p.385-398).

Jones discloses experimental examination of a targeted hyperthermia system using inductively heated ferromagnetic microspheres in rabbit kidney (page 385). Magnetic particles are incorporated into the matrix of a larger, less dense microsphere. Microspheres are manufactured from a biocompatible polymer known as Biopol using a solvent evaporation technique. Magnetic particles (Fe_2O_3) are first dispersed in Biopol that has been dissolved in dichloromethane. This solution is then dispersed in water containing 0.25% high molecular weight PVA and mixed with a high-speed mixer to evaporate, leaving the solidified biopol microspheres containing Fe_2O_3 particles. Micrspheres are seived to select those in the size range 25-40 micron, with average size of 32 micron. Microspheres of average density 1.6, 2.3 and 2.8 g/cm^3 were selected and used (page 388). Table 1 describes the details of administered

microspheres including dose, density, concentration of Fe_2O_3 in tissue and effective SAR mW g^{-1}).

Jones does not explicitly recite that the magnetic material is in the form of nanoparticles.

Lesniak discloses nanoscale particles suited for use in tumor therapy by hyperthermia. Said particles comprise a preferably superparamagnetic iron oxide containing core and at least two shells surrounding said core (abstract). Iron oxide-containing core includes magnetite, maghemite, etc. and core has an average particle size of 3 to 30 nm (claims 5, 7).

Handy discloses therapeutic methods for treatment of disease material involving administration of a thermotherapeutic magnetic composition, which contains single domain magnetic particles attached to a target-specific ligand, to a patient and application of an alternating magnetic field to inductively heat the thermotherapeutic magnetic composition (abstract). The term "bioprobe" refers to the composition comprising a magnetic particle, a biocompatible coating material, and a target-specific ligand (column 6, lines 1-5). Alternating magnetic field frequency is preferably between 100-500 kHz (column 7, line 58 – column 8, line 50). AMF strength is between 20 and 3000 Oe, more preferably 100 and 2000 Oe (column 9, lines 20-25). The size of the magnetic particle such as magnetite (Fe_3O_4) may be from 8 to 20 nm. The size fo the bioprobe may be 250 nm (column 12, lines 34+). Suitable materials for coating include synthetic and biological polymers such as acrylates, siloxanes, styrenes, acetates, alkylene glycols, etc. (column 13, lines 5-55). See also Examples 1-22, including

FMn2X ferromagnetic particles, poly(methacrylic acid-co-hydroxyethylmethacrylate) coating, dextran shell, etc.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ nanoscale maghemite particles, such as particles less than 30 nm in size in the methods of Jones when the teaching of Jones is taken in view of Lesniak and Handy. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so because Jones teaches that gamma ferric oxide, Fe_2O_3 is used as the magnetic material, and because Lesniak teaches that particle size of not more than 30 nm is usually a prerequisite for superparamagnetism (column 3, lines 60+). With regard to claimed frequency and field strength of the alternating magnetic field used in hyperthermia treatment, Handy shows frequency and field strength known in the art to be useful for such methods. Regarding claims 2-4, while Jones does not specifically recite percentage of maghemite in the microspheres, it is interpreted absent evidence to the contrary that the microspheres of Jones would inherently be capable of having the claimed volume fraction of magnetic material and would be capable of achieving the claimed value because Jones teaches particles having the same material components and same density (e.g. 1.8-2.8 g/cm^3. Since the density of the particles is directly related to the respective amounts of magnetic particle and matrix polymer present within the microcapsule, a microcapsule comprising the same materials (e.g. maghemite and biopol or PVA) and having the same size and density would thus have the claimed volume fraction of magnetic material. Regarding claim 10, Jones teaches microspheres having the same size, density, and material

components as those claimed and exemplified in Applicant's specification (e.g. maghemite and biopol or PVA), thus absent evidence to the contrary the microcapsules would inherently be capable of achieving the claimed VAR values upon exposure to alternating magnetic field. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618
LHS